



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/904,532 | 07/13/2001 | Napoleone Ferrara | 10466/50 | 2313 |
| 35489 | 7590 | 01/20/2006 | EXAMINER | |
| HELLER EHRLMAN LLP 275 MIDDLEFIELD ROAD MENLO PARK, CA 94025-3506 | | | DEBERRY, REGINA M | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1647 | |
| DATE MAILED: 01/20/2006 | | | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|-------------------|---------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/904,532 | FERRARA ET AL |
| | Examiner | Art Unit |
| | Regina M. DeBerry | 1647 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 01 November 2005.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 39-47 and 49-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) 42-47 and 49 is/are allowed.
- 6) Claim(s) 39-41, 50 and 51 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____. |

Status of Application, Amendments and/or Claims

The amendment filed 01 November 2005 has been entered in full. Claims 39-47 and 49-51 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection to claims 39 and 44 under 35 USC 112, second paragraph, as set forth at pages 7-8 of the previous Office Action (01 August 2005), is *withdrawn* in view of Applicant's argument (01 November 2005).

The rejection to claims 39-47 under 35 USC 112, second paragraph, as set forth at page 8 of the previous Office Action (01 August 2005), is *withdrawn* in view of the amendment (01 November 2005).

The rejection to claim 44 under 35 USC 112, second paragraph, as set forth at page 8 of the previous Office Action (01 August 2005), is *withdrawn* in view of Applicant's argument (01 November 2005).

Claim Objections

The disclosure remains objected to because of the following informalities: The phrase "Table 7 (cont.)" appears inappropriately in the middle of pages 219-221. The

disclosure contains blank spaces and/or pages (pages 65, 90, 94-98). The basis for this rejection is set forth at pages 2-3 of the previous Office Action (01 August 2005).

This objection was not addressed. The objection is still maintained.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 39-41, 50 and 51 remain rejected under 35 U.S.C. 112, first paragraph, enablement. The basis for this rejection is set forth at pages 3-5 of the previous Office Action (01 August 2005).

Applicant argues that they do not predict protein structure from sequence data and that the claimed variants all share the functional recitation that, "said polypeptide inhibits VEGF stimulation of endothelial cell growth". Applicant cites Example 66 in the instant specification. Applicant argues that structurally related or unrelated polypeptides would not be encompassed by the instant claims because Applicants claim only those proteins which meet both recitations of the claims, structural and functional. Applicant maintains that the specification describes methods for determination of percent identity between two amino acid sequences. Applicant cites pages in the instant specification. Applicant argues that biological activity in this instance is not claimed based on structural similarity, but instead based on the positive results in the inhibition of VEGF stimulation of endothelial cell growth assay.

Applicant's arguments have been fully considered but are not deemed persuasive. The Examiner agrees that the instant protein has the activity of inhibiting

VEGF stimulation of endothelial cell growth. However, there are no working examples of polypeptides *less than 100% identical* to the polypeptide (SEQ ID NO:127), wherein said polypeptide inhibits VEGF stimulation of endothelial cell growth. The specification fails to teach (i) which portions of SEQ ID NO:127 are critical to the activity of the protein of SEQ ID NO:127; and (ii) what modifications (e.g., substitutions, deletions or additions) one can make to SEQ ID NO:127 will result in protein mutants with the same functions as the protein of SEQ ID NO:127. The Examiner cited Wells to show that the state of the art is such that the relationship between sequence of a protein and its activity is not well understood and is not predictable. Excising out portions of a protein or modifications to a protein, e.g., by substitutions or deletions, would often result in deleterious effects to the overall activity and effectiveness of the protein. The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. Lack of a working example, however is a factor to be considered, especially in a case involving an unpredictable and undeveloped art.

Accordingly, the disclosure fails to enable such a myriad of the claimed polypeptide molecules that not only vary substantially in length but also in polypeptide composition and to provide any guidance to those skilled generally on how to make and use the claimed genus of polypeptide molecules. Thus, it would require undue experimentation for one skilled in the art to make and use the claimed genus of polypeptide molecules embraced by the instant claim. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

Claims 39-41, 50 and 51 remain rejected under 35 U.S.C. 112, first paragraph, written description. The basis for this rejection is set forth at pages 5-7 of the previous Office Action (01 August 2005).

Applicant argues that Example 66 of the present application provides detailed protocols for the VEGF stimulation of endothelial cell growth assay, including the extensive step-by-step guidance in the specification. Applicant argues that the specification describes methods for the determination of percent identity between two amino acid sequences. Applicant cites various pages in the instant specification.

Applicant's arguments have been fully considered but are not deemed persuasive. Applicant is invited to visit the PTO Website for the most currently published version of the Written Description Guidelines Material (Example 14). The instant specification contemplates but does not exemplify variants of the protein wherein the variant can have unspecified substitutions, deletions, insertions and/or additions in SEQ ID NO:127, wherein said polypeptide inhibits VEGF stimulation of endothelial cell growth. The specification states that these types of changes are routinely done in the art and provides a table of potential amino acid substitutions. The specification does not provide any guidance as to what changes should be made and which regions of the instant protein are functionally and structurally critical. There is no description of variants of SEQ ID NO:127 that exist, while still maintaining function. There is no identification of any particular portion of the structure that must be conserved in order to

conserve the required function. The specification only shows possession of a single species.

The courts have specifically stated that the skilled artisan cannot envision the *detailed chemical structure* of an encompassed polypeptide until the structure is disclosed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In the instant case, SEQ ID NO:127 has been disclosed, but no native sequence variants thereof have been disclosed regardless of whether or not they inhibit VEGF stimulation of endothelial cell growth. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. There is no identification of any particular portion of the structure that must be conserved in order to conserve the required function. Clearly, such does not constitute disclosure of a representative number of examples of, nor adequate written description for, the claimed genus. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Conclusion

Claims 39-41, 50 and 51 are rejected.

Claims 42-47, 49 are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RMD
1/17/05

Marianne P. Allen
MARIANNE P. ALLEN
PRIMARY EXAMINER
1/18/06

441647